

**PATENT**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**  
**(Case No. 96,725-C)**

In re Application of: )  
 )  
FLAVIN ET AL. )  
 ) Group Art Unit: 2673  
Serial No.: Not Yet Assigned )  
 ) Examiner: Dr. Jones  
Filed: December 14, 2000 )  
 )  
For: USE OF AUTOMATED )  
TECHNOLOGY IN CHEMICAL )  
PROCESS RESEARCH AND )  
DEVELOPMENT )

Asst. Commissioner for Patents  
Washington, DC 20231

**PRELIMINARY AMENDMENT**

Dear Sir:

Please enter the following preliminary amendment in the above-referenced patent application.

**IN THE SPECIFICATION**

At page 3, line 12, change "FIGURE 5 is" to --FIGURES 5A-5G are--, such that the sentence reads "FIGURES 5A-5G are an additional flow chart of the sequence of steps in performing the preferred chemical reaction optimization routine using the equipment of FIGURE 1."

At page 5, line 12, change "synthesizer 42" to --synthesizer 12--, such that the sentence reads "The computer 42 regulates the environmental conditions in the synthesizer 12 such as by controlling the temperature of the wells 16."

At page 8, line 15, insert --, as shown at block 58 of Figure 3,-- after “step 4”, such that the sentence reads “Once the 48 reactions are completed, at step 4, as shown at block 58 of Figure 3, the tasks of compound analysis and data compilation begin.”

At page 9, line 11, change "arrow 50" to --arrow 51--, such that the sentence reads "This is represented by the arrow 51 in Figure 3."

At page 9, line 18, change “FIGURE 5 is” to --FIGURES 5A-5G are--, such that the sentence reads “FIGURES 5A-5G are an additional flow chart of the sequence of steps in performing the preferred chemical reaction optimization routine.”

At page 9, line 24, change “FIGURE 5” to --FIGURES 5A-5G--, such that the sentence reads “As shown in FIGURES 5A-5G, the total number of wells is designated as “X.”

At page 10, line 5, insert --, as shown at block 86 of Figure 5-- after “synthesizer 12”, such that the sentence reads “The pipetting mechanism 74 then stores the reagents in the dispenser of the drive of the synthesizer 12, as shown at block 86 of Figure 5”.

At page 10, line 5, insert --, with the well\_number set equal to 1, as shown at block 88 of Figure 5-- after “wells 16”, such that the sentence reads “Then a loop is executed for each of the wells 16, with the well\_number set equal to 1, as shown at block 88 of Figure 5”.

At page 10, line 8, insert --, as shown at block 94 of Figure 5-- after “the well”, such that the phrase reads “the well, as shown at block 94 of Figure 5”.

At page 10, line 11, insert --The well\_number is incremented by 1, as shown at block 96 of Figure 5. If the well\_number is greater than the total number of wells (X), then the loop is exited, as shown at block 98 of Figure 5. Otherwise, the flow chart of Figure 5 goes to block 90.-- after “described subsequently.”, such that the sentences read “The reagents values and type of reagents is either based on operator input or based on the optimization scheme described subsequently. The well\_number is

incremented by 1, as shown at block 96 of Figure 5. If the well\_number is greater than the total number of wells (X), then the loop is exited, as shown at block 98 of Figure 5. Otherwise, the flow chart of Figure 5 goes to block 90.”

At page 10, line 22, insert --, as shown at block 102 of Figure 5. The well\_number is set equal to 1, as shown at block 104 of Figure 5-- after “argon gas”, such that the phrase reads “argon gas, as shown at block 102 of Figure 5. The well\_number is set equal to 1, as shown at block 104 of Figure 5”.

At page 11, line 3, insert --The well\_number is incremented by 1, as shown at block 112 of Figure 5. If the well\_number is greater than the total number of wells (X), then the loop is exited, as shown at block 114 of Figure 5. Otherwise, the flow chart of Figure 5 goes to block 108.-- after “temperature value 110.”, such that the sentences read “The processor 64 sends a command to the temperature control system 18 to set the temperature value 110. The well\_number is incremented by 1, as shown at block 112 of Figure 5. If the well\_number is greater than the total number of wells (X), then the loop is exited, as shown at block 114 of Figure 5. Otherwise, the flow chart of Figure 5 goes to block 108.”

At page 11, line 6, insert --, as shown at block 116 of Figure 5-- after the first occurrence of “same rate”, such that the sentence reads “The agitation/mixing of the synthesizer is next initialized based on whether the individual wells are mixed at different rates or whether the entire reaction block is agitated at the same rate, as shown at block 116 of Figure 5.”

At page 11, line 8, insert --, with the well\_number set equal to 1 as shown at block 122 of Figure 5,-- after “enters a loop”, such that the sentence reads “If the agitation is at different rates, the program enters a loop, with the well\_number set equal to 1 as shown at block 122 of Figure 5, and determines the agitation from the parameter look-up table for each well 124 and sends a command to the agitator/mixer 126.”

At page 11, line 10, insert --The well\_number is incremented by 1, as shown at block 128 of Figure 5. If the well\_number is greater than the total number of wells (X), then the loop is exited, as shown at block 130 of Figure 5. Otherwise, the flow chart of Figure 5 goes to block 124.-- after "agitator/mixer 126.", such that the sentences read "agitator/mixer 126. The well\_number is incremented by 1, as shown at block 128 of Figure 5. If the well\_number is greater than the total number of wells (X), then the loop is exited, as shown at block 130 of Figure 5. Otherwise, the flow chart of Figure 5 goes to block 124."

At page 11, line 11, insert --, as shown at block 132 of Figure 5, -- after "the wells", such that the sentence reads "The reaction times are then determined for each of the wells, as shown at block 132 of Figure 5, based on the data in the parameter look-up table."

At page 11, line 12, insert --in an array-- after "are ordered", such that the phrase reads "The wells are ordered in an array".

At page 11, line 13, change "highest 134" to --highest with a pointer set to the first item in the array, as shown at block 134 of Figure 5. The reaction time is determined for the well which is at the pointer, as shown at block 136--, such that the sentence reads "The wells are ordered in an array based on reaction time, from lowest to highest with a pointer set to the first item in the array, as shown at block 134 of Figure 5. The reaction time is determined for the well which is at the pointer, as shown at block 136."

At page 11, line 15, insert --as shown at block 140,-- after "particular well, ", such that the sentence reads "When the reaction time has been exceeded for a particular well, as shown at block 140, the reaction is stopped 142."

At page 11, line 18, insert --The pointer is set to the next item in the array, as shown at block 144. As shown at block 146, if the pointer is outside of the array, the flow chart goes to block 148. Otherwise, the flow chart goes to block 136.-- after "stop the reaction.", such that the sentences read "may be added

to stop the reaction. The pointer is set to the next item in the array, as shown at block 144. As shown at block 146, if the pointer is outside of the array, the flow chart goes to block 148. Otherwise, the flow chart goes to block 136.”.

At page 11, line 19, insert --If yes, the block is quenched, as shown at block 150.-- after “the entire reaction block 148.”, such that the sentences reads “Then, based on the parameter look-up table 69, the processor determines whether to quench the entire reaction block. If yes, the block is quenched, as shown at block 150.”

At page 11, line 21, insert --The well\_number is set equal to 1, as shown at block 152 of Figure 5.-- after “and analyzed.”, such that the sentences read “After the reaction, the components of each of the wells 16 must be removed from each of the wells, sent to the analyzer 40 and analyzed. The well\_number is set equal to 1, as shown at block 152 of Figure 5.”

At page 11, line 24, insert --, as shown at block 160, -- after “the reaction mixture”, such that the phrase reads “The analyzer 40 then analyzes the components of the reaction mixture, as shown at block 160, and sends the results”.

At page 12, line 1, insert --, as shown at block 162 -- after “the wells”, such that the sentence reads “The processor 64 examines the data from the analyzer 40 and, based on a product table, determines the products of the yield in each of the wells, as shown at block 162.”

At page 12, line 5, insert --, as shown at block 164, -- after “newly-created table”, such that the sentence reads “The processor stores the analysis in a newly-created table, as shown at block 164, and continues obtaining data for each of the wells.”

At page 12, line 5, insert --The well\_number is incremented by 1, as shown at block 166 of Figure 5. If the well\_number is greater than the total number of wells (X), then the loop is exited, as shown at block 168 of Figure 5. Otherwise, the flow chart of Figure 5 goes to block 154.-- after “the wells.”, such

that the sentences read “The processor stores the analysis in a newly-created table and continues obtaining data for each of the wells. The well\_number is incremented by 1, as shown at block 166 of Figure 5. If the well\_number is greater than the total number of wells (X), then the loop is exited, as shown at block 168 of Figure 5. Otherwise, the flow chart of Figure 5 goes to block 154.”

At page 14, line 17, insert --The well\_number is set equal to 1, as shown at block 170. The well\_number is incremented by 1, as shown at block 176 of Figure 5. If the well\_number is greater than the total number of wells (X), then the loop is exited, as shown at block 178 of Figure 5. Otherwise, the flow chart of Figure 5 goes to block 174.-- after “tallied 174.”, such that the sentence reads “Each of the results for an individual well can then be tallied 174. The well\_number is set equal to 1, as shown at block 170. The well\_number is incremented by 1, as shown at block 176 of Figure 5. If the well\_number is greater than the total number of wells (X), then the loop is exited, as shown at block 178 of Figure 5. Otherwise, the flow chart of Figure 5 goes to block 174.”

**IN THE FIGURES:**

Please amend Figure 3:

As shown in the enclosed amended Figure 3, add --51--.

Please amend Figure 5:

As shown in the enclosed amended Figure 5, change “FIG. 5” to --FIG. 5A--.

As shown in the enclosed amended Figure 5, add --FIG. 5B-- at the bottom of page 2 of Figure 5.

As shown in the enclosed amended Figure 5, add --FIG. 5C-- at the bottom of page 3 of Figure 5.

As shown in the enclosed amended Figure 5, add --FIG. 5D-- at the bottom of page 4 of Figure 5.

As shown in the enclosed amended Figure 5, add --FIG. 5E-- at the bottom of page 5 of Figure 5.

As shown in the enclosed amended Figure 5, add --FIG. 5F-- at the bottom of page 6 of Figure 5.

As shown in the enclosed amended Figure 5, add --FIG. 5G-- at the bottom of page 7 of Figure 5.

**IN THE CLAIMS:**

Please cancel claims 1-5 without prejudice.

Please add the following new claims 6-22 as follows:

6. (New claim) In a method for optimizing chemical synthesis using a synthesizer, an analyzer, and a computer, the method including the steps of: (a) identifying variables which affect chemical synthesis for a reaction; (b) choosing a finite number of experimental tests, wherein the experimental tests have values for the variables; (c) providing a plurality of wells; (d) assigning each of the experimental tests to a particular well; (e) synthesizing samples in the synthesizer using the values in the experimental tests; (f) obtaining at least portions of the samples from the plurality of wells; (g) analyzing the portions of the samples using the analyzer to determine amounts of at least one component in each of the samples, the improvement comprising the steps of:

automatically generating a statistical analysis using the computer based on the amounts of the at least one component in the samples and at least one of the variables identified in order to evaluate the reactions in the wells; and

automatically generating, using the computer, suggested parameters for future experiments based on the statistical analysis.

7. (New claim) The method as claimed in claim 6 wherein the variables include operating conditions and reagent concentrations.

8. (New claim) The method as claimed in claim 7 wherein the variables further include reaction times.

9. (New claim) The method as claimed in claim 6 further comprising the step of determining a range of values of the variables.

10. (New claim) The method as claimed in claim 9 wherein the values for the experimental tests are chosen from the range of values.

11. (New claim) The method as claimed in claim 10 wherein the values for the experimental tests are chosen randomly from the range of values.

12. (New claim) The method as claimed in claim 10 wherein the suggested parameters are chosen from a new range of values, the new range of values being narrower than the range of values.

13. (New claim) The method as claimed in claim 6 wherein the step of automatically generating a statistical analysis includes determining a most favorable reaction in one of the plurality of wells based on the amounts of the at least one component and the at least one variable.



14. (New claim) The method as claimed in claim 6 wherein the step of automatically generating a statistical analysis includes graphically describing the reactions in the plurality of wells based on the amounts of the at least one component and the at least one variable.

15. (New claim) The method as claimed in claim 14 wherein graphically describing the reactions includes generating multivariable contour maps.

16. (New claim) The method as claimed in claim 6 further comprising the steps of:  
dispensing reagents into the plurality of wells using the suggested parameters;  
reacting in the synthesizer the reagents using the suggested parameters;  
obtaining samples from the plurality of wells; and  
analyzing the samples using the analyzer to determine amounts of at least one component in each of the samples.

17. (New claim) In a method for optimizing chemical synthesis using a synthesizer, an analyzer, and a computer, the method including the steps of: (a) identifying variables which affect chemical synthesis for a reaction; (b) determining a range of values of the variables; (c) choosing a finite number of experimental tests, wherein the experimental tests have values for the variables chosen from the range of values; (d) providing a plurality of wells; (e) assigning each of the experimental tests to a particular well; (f) dispensing reagents into a plurality of wells chosen from the values for the experimental tests; (g) reacting in the synthesizer the reagents using operating conditions chosen from the values for the experimental tests; (h) obtaining samples from the plurality of wells; (i) analyzing the

samples using the analyzer to determine amounts of at least one component in each of the samples, the improvement comprising the steps of:

automatically generating a statistical analysis using the computer based on the amounts of the at least one component in the samples and at least one of the variables identified in order to evaluate the reactions in the wells;

automatically generating suggested parameters for future experiments using the computer wherein the suggested parameters are chosen from a new range of values based on the statistical analysis in order to optimize chemical synthesis, the new range of values being different from the range of values;

dispensing reagents into the plurality of wells using the suggested parameters;

reacting in the synthesizer the reagents using the suggested parameters;

obtaining samples from the plurality of wells; and

analyzing the samples using the analyzer to determine amounts of at least one component in each of the samples.

18. (New claim) The method as claimed in claim 17 wherein the step of automatically generating a statistical analysis includes ranking the plurality of wells based on the amounts of the at least one component the at least one variable.

19. (New claim) The method as claimed in claim 17 wherein the step of automatically generating a statistical analysis includes determining a most favorable reaction in one of the plurality of wells based on the amounts of the at least one component and the at least one variable.

20. (New claim) The method as claimed in claim 17 wherein the step of automatically generating a statistical analysis includes graphically describing the reactions in the plurality of wells based on the amounts of the at least one component and the at least one variable.

21. (New claim) The method as claimed in claim 20 wherein graphically describing the reactions includes generating multivariable contour maps.

22. (New claim) The method as claimed in claim 17 wherein the new range of values is narrower than the range of values.

#### **REMARKS**

Applicants submit this preliminary amendment in order to amend the specification and figures and to add new claims. In particular, Applicants have amended the specification where it is believed appropriate based on the prosecution of the parent case (Application Serial No. 08/862,840). For example, the amendments to the specification are the same amendments that were submitted on January 11, 1999 in response to an Office Action mailed July 10, 1998. Moreover, the amendments to the figures are the same as those submitted in the January 11, 1999 amendment and the amendment after notice of allowance dated November 3, 1999.

Applicants have also presented new claims that define over the references of record. It is submitted, therefore, that the Application is in condition for allowance and early notice to this effect is earnestly solicited.

If for any reason, the application is not considered to be in condition for allowance on the next Office Action and an interview would be helpful to resolve any remaining issues, the Examiner is requested to contact the undersigned attorney at (312) 913-0001.

Respectfully submitted,

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